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REMARKS

This application is a continuation of serial no. 09/866,443. Claims 1-16 were present in the application when filed. In response to an Office Action dated April 25, 2005, claim 1 was amended. Claims 1-16 remain pending in the application.

Rejection under 35 U.S.C. §102

Claims 1 and 7-16 are rejected under 35 U.S.C. §102(b) as being anticipated by Oldroyd et al. (Aust J. Agric Res, 1989, 40(3). p. 691-698.) According to the Office Action, the rejection was on the grounds that Oldroyd et al. teach that honeybee colonies were treated with various oxytetracycline hydrochloride (OTC) preparations at the same time of inoculation with Bacillus larvae spores, thereby anticipating a composition as claimed by Applicants. The Office Action further states that "Oldroyd teaches a composition comprising Bacillus larvae... that were American Foubrood (AFB) disease-free at the time of sampling and did not subsequently develop disease signs." From this, the Office Action concludes that Oldroyd teaches Applicants' claimed composition. Applicants respectfully submit that a proper reading of Oldroyd makes it clear that B. larvae is not, as the Office Action maintains, non-pathogenic to bees. Oldroyd, therefore, cannot anticipate the present invention.

Independent claim 1 of the instant application, as previously presented, recites a composition for the treatment or prophylaxis of a bee disease, the composition comprising: a) an inoculum containing one or more microorganisms that are non-pathogenic to bees for producing a microflora having therapeutic or prophylactic efficacy against the bee disease; and b) an apicultural delivery vehicle for delivering the inoculum to a component of a bee hive, or to a bee colony that is susceptible to or infected with the bee disease, whereby a remedial and/or protective microflora is established within the hive or the bee colony. Thus, a primary feature of the claimed composition is an inoculum of one or more microorganisms that are non-pathogenic to bees.

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A proper reading of Oldroyd would not lead one of skill in the art to conclude that B. larvae is a non-pathogenic organism. In direct contrast, Oldroyd teaches that Bacillus larvae is a pathogenic organism, administered to induce disease. Oldroyd presents the results of a study of the effect of oxytetracycline hydrochloride treatment on American foulbrood. In these studies, honeybee colonies were treated with oxytetracycline hydrochloride preparations at the time that the colony was inoculated with Bacillus larvae spores to induce the disease or after American foulbrood disease signs had developed. Not surprisingly, Oldroyd (abstract) states that B. larvae was subsequently cultured from adult bee samples from colonies that did not develop disease signs. These colonies, however, were treated with OTC. Oldroyd does not suggest that these colonies are disease free subsequent to inoculation with B. larvae because is not a pathogen; rather, Oldroyd concludes that these results show that recommended treatments for European foulbrood (EFB), i.e., treatment with OTC, essentially suppress signs of AFB disease.

The relevant portion of Oldroyd appears on page 693 and reads as follows: "Experiment 1: Effects of OTC as a Preventative of AFB Disease

All control colonies [emphasis added] inoculated with B. larvae spores developed disease signs within 40 days (Fig.1). OTC treatment at the time of inoculation prevented the development of disease signs for 58 days in one hive, 291 days in another hive and two other colonies became diseased in mid-summer, more than 1 year after their inoculation with B. larvae spores. AFB disease was prevented by OTC treatment at the time of inoculation in 1 colony only (Fig.1)."

Thus, all of the control colonies, that is, those receiving B. larvae spores in the absence of OTC, developed disease signs. Of the colonies inoculated with B. larvae and treated with OTC, only one colony was disease-free at the time of sampling. The absence of signs of disease in this single colony does not indicate that B. larvae is non-pathogenic, rather, it is due to the fact that the colony was successfully treated with OTC, an antibacterial agent effective against B. larvae.

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Applicant does not disagree with the definition of non-pathogenic put forth in the Office Action. Applicants do, however, dispute the Office Action's characterization of B. larvae as a non-pathogenic organism rather than a pathogenic one (See Annex A for the definition of pathogen.) There is no evidence in the prior art to suggest that Bacillus larvae is a nonpathogenic strain of bacteria. Rather, the relevant literature, including Oldroyd, teaches that American foulbrood (AFB) is caused by B. larvae (now known as Paenibacillus larvae subsp. larvae). The literature also teaches that oxytetracycline hydrochloride (OTC) therapy is commonly used to control American foulbrood (AFB). In support of this position, Applicants submit three additional documents, labeled Annex B-D. Annex B, an abstract from a report by Genersch et al. entitled "Strain- and Genotype-Specific Differences in Virulence of Paenibacillus larvae subsp. larvae, a Bacterial Pathogen Causing American Foubrood Disease in Honeybees," unequivocally identifies Paenibacillus larvae subsp. larvae as the causative agent of American foulbrood disease. Annex C, the abstract from a report from Rural Industries Research and Development Corporation of the Australian government, on oxytetracycline sensitivity of Paenibacillus larvae subsp. larvae isolates states that American foulbrood (AFB) is caused by Paenibacillus larvae subsp. larvae and establishes that P. larvae subsp. larvae isolated from Australian sources are very sensitive to OTC. Lastly, an entry from DSMZ, Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, clearly identifies Paenibacillus larvae subsp. larvae (synonym Bacillus larvae) as an animal pathogen (Annex D).

It necessarily follows that, inoculation of a bee colony with *B. larvae* would not be able to produce a microflora having therapeutic or prophylactic efficacy against the bee disease, as recited by independent claim 1. Indeed, Oldroyd does not teach the establishment of a protective microflora within the hive or bee colony.

Treatment or prevention of bee disease by Applicant's claimed composition is achieved either by the non-pathogenic microorganism producing an antibiotic against a pathogenic microorganism or by a population of the non-pathogenic microorganism competing with

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pathogenic microorganisms and preventing infection thereby. This is discussed on page 3 of the description.

Lastly, it is well established that a preamble that "breathes life and meaning into the claim is a necessary limitation to them." In the present case, the claimed composition is for the treatment or prophylaxis of a bee disease. In view of the clear teachings of Oldroyd that colonies were inoculated with B. larvae for the purpose of inducing foulbrood disease, one of skill in the art would appreciate that Oldroyd cannot anticipate Applicants claimed composition for the treatment of the disease.

Having clearly established that Bacillus larvae (now known as Paenibacillis larvae subsp. larvae) is a pathogenic rather than a non-pathogenic organism, Applicants' respectfully submit that the claimed composition comprising an inoculum of non-pathogenic microorganism is in stark contrast to the compositions of the cited references which contain an inoculum of the pathogen for inducing disease which applicants' claimed composition seeks to treat or prevent. Therefore, Oldroyd et al teaches inoculation with a microorganism that is pathogenic to bees and, as such, Oldroyd cannot anticipate Applicants' invention.

Claims 1 and 7-16 are further rejected under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious by Hoopingarner et al. (American Bee Journal, 1988, Vol. 128, No. 2, p. 120-121).

Hoopingamer, like Oldroyd, teaches inoculation with *B. larvae* pathogen for the purpose of inducing American foulbrood disease to evaluate the effectiveness of three terramycin formulations on that disease.

The relevant portion of Hoopingamer appears on page 120 and reads as follows: "Three weeks after the nucs were established, they were inoculated with AFB [emphasis added] by spraying them with syrup containing a heavy concentration of *B. larvae* spores.

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After four weeks to allow the disease to become established, the treatment each nuc was to receive was chosen randomly."

For the reasons given above with respect to the teachings of Oldroyd, Hoopingamer does not teach or fairly suggest a composition comprising an inoculum of non-pathogenic microorganisms for the prevention of *B. larvae* induced foulbrood disease. Furthermore, the teachings of Hoopingamer do not compensate for the shortcomings of Oldroyd. The combination of the references does not teach Applicants' claimed composition.

Withdrawal of the rejection under 35 U.S.C. §§ 102/103 is respectfully requested.

For the foregoing reasons, the claims are believed in condition for allowance and such action is respectfully requested. The dependent claims are believed allowable for the same reasons as the independent claims from which they ultimately depend, as well as for their additional limitations.

Should the Examiner require clarification of any of the above, she is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Reg. No. 41,707

Dated: January 19, 2006

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ANNEX A

patch board

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pathology

together temporarily by means of a patch board. 20. (usually foll. by through) to connect (a telephone call) by means of a patch board. 21. Computer technol to correct or improve (a program) by

adding a small set of instructions. [Cle pacche, perhaps from French pieche PECE] — patchable ed. — patcher n. patch board or panel n. a device with a large number of sockets into which electrical plugs can be inserted to form many different temporary circuits; used in telephone exchanges, computer systems, etc. Also called: plughourd.

patchoull, pachoull, or patchouly ('perful, po'thull) n. I. any of several Asiatic trees of the ganus Pogastumon, the leaves of which yield a heavy fragrant oil: family Labiette (labiates). 2. the perfume made from this oil. [C19: from Tamil paccilal, from paccu green + ilei leaf)

paich pocket n. a pocket on the outside of a garment.

patch quit a. Irish a patchwork quit.

patch test n. Med a test to detect an allergic reaction by applying small amounts of a suspected substance to the skin and then examining the area for signs of fritation.

pairinwork ('patf.watk) n. 1. needlework done by sewing pieces of different materials together. 2. something, such as a theory, made up of various parts: a patchwork of cribbed ideas.

patchy ('petil') adi. patchier, patchiest. 1. irregular in quality, occurrence, intensity, etc.: a patchy essay. 2. having or forming patches. — patchily adv. — patchinese a.

paid abbrev, for patented. pain (post) A. the head, esp. with reference to baldness or (in facetious use) intelligence. (C14: of unknown origin)

pâte ('pæter French pate) n. l. a spread of very finely minced liver, poultry, etc., served usually as an hors d'ocuvre. L a savoury pie of meat or fish. [from French: PASTE']

pâté de foie graz (pote de fwa gro) n. pt pâtés de foie graz (pote de fwa gro). A smooth rich paste made from the liver of a specially fattened goose, considered a great delicecy. [French: pâté of fat

patella (pettele) n., pl. -lee (-li:). 1. Anatomy, a small flat triangular bone in front of and protecting the knee joint. Nontechnical name: knoocap. 2. Blology, a cublike structure, such as the sporeproducing body of certain ascomycetous fungi. 3. Archaeol a small pan. [C17: from Latin, from paties shallow pan] —patcellar adj. patellate (poltclit, -,leit) ad/, having the shape of a patella. Also:

patelilform (pateli,fam). paten ('pat'n), patin, or patine ('patin) n. a plate, usually made of sliver or gold, esp. the plate on which the bread is placed in the Eucharist. [C13: from Old French patene, from Medieval Latin, from Latin petine pan]

patency ('pen'ast) n. 1. the condition of being obvious. 2. the state of a bodily passage, duct, etc., of being open or unobstructed. 2. Phonecies the degree to which the vocal tract remains unobstructed in the articulation of a speech sound. See also closure (sense 6). Pateniar л. Josephin. See (Josephin) Patinir.

patent ('part'at, 'part'at) n. 1. a. a government grant to an inventor assuring him the sole right to make, use, and sell his invention for a limited period. b. a document conveying such a grant. 2. an invention, privilege, etc., protected by a patent. 2. a. an official document granting a right, b. any right granted by such a document. 4. (In the U.S.) a. a grant by the government of title to public lands. b. the instrument by which such title is granted, c. the land so b. the instrument by which such this is granted. c. the land so granted. 5. a sign that one possesses a certain quality. ~adj. 6. open or available for inspection (esp. in the phrases letters patent. patent writ). 7. ('pen'nt). obvious their scorn was patent to everyone. 8. concerning protection, appointment, etc., of or by a patent or patents. 9. proprietary. 19. (esp. of a bodily passage or duct) being open or unobstructed. 11. Biology, spreading out widely, patent branches. 12. (of plate glass) ground and polished on both sides. -vb. (cr.) 18. to obtain a patent for. 14. (in the U.S.) to grant (public land or mineral rights) by a patent. 15. Metallurgy, to heat (a metal) above a transformation temperature and cool it at a rate that allows cold working. [C14: via Old French from Latin patere to lie open; n. use, short for letters patent, from Medieval Latin litterus patentes letters lying open (to public inspection)] ·'patentable adj. —,patenta'bility o.

Usage. The pronunciation "ipperni" is heard in letters patent and Patent Office and is the usual U.S. promunciation for all senses. In Britain "'pet'nt" is sometimes heard for senses 1, 2 and 3, but "'pett'nt" is commoner and is regularly used in collocations like patent leather.

patentee (,pan'n'tli, ,pæ-) n. a person, group, company, etc., that has been granted a patent.

patent fastener s. (In Ireland) another name for press stud.

patent leather n. leather or imitation leather processed with lacquar to give a bard glossy surface.

paient top a. Neutical, any of several mechanical devices for measuring the speed of a vessel and the distance travelled, consisting typically of a trailing rotor that registers its rotations on a meter. Compare chip los.

patently ('pen'ntil) adv. obviously: he was patently bored. patent medicine a. a medicine, usually of low potency, protected by a patent and available without a doctor's prescription.

Palant Office ('pat'at) a. a government department that issues patents. Abbrev.: Pat. Off. patentor (,peit ntm. ,ps-) n a person who or official body that

grants a patent or patents.
patent right in the exclusive right granted by a patent.
Patent Rolls pt n. (in Britain) the register of patents issued.

patent still a. a type of still in which the distillation is continuous. [so called because a still of this type was patented in 1830]

pater ('pens) a. Bris. a public school slang word for fathers now chiefly used facatiously. [from Latin]

Poter ('petto) n. Waiter (Horatio). 1839-94, English ossayist and a critic, noted for his proce style and his advocation of the "love of any for its own sake". His works include the philosophical rotation Marius the Epicurean (1885), Studies in the History of the Rensipsance (1873), and Imaginary Portraits (1887).

pateriamilias ("pertoro mili, 23) n., pl. patresfamilias ("potremo...
imili, 23). 1. the male head of a household. 2. Roman law. a. the,
head of a household having authority over its mombers. h. the parental or other authority of another person. [Latin: father of the

paismal (po'tain) adi. 1. relating to or characteristic of a father, esp. in showing affection, oncouragement, etc.; fatherly. 2. (Are nominal) related through the father: his paternal grandfather. 2. Inherited or derived from the male parent. [C17: from late Latin paternalls, from Latin pater father] —pa'tornally adv.

paternalism (po'tama,lizam) n. the attitude or policy of a government or other authority that manages the affairs of a country company, community, etc., in the manner of a father, esp. in

paternity (poltanno) n. 1. a. the fact of state of being a father, b. (as modifier); a paternity suit was filed against the man. 2 descent or derivation from a father. 3. authorship or origin; the paternity of the theory is disputed. [Cl5; from Late Latin paternips, from Latin

paternity suit n. Law. the U.S. (and in Britain a nontechnical) term for affiliation proceedings.

palernoster (,pato nesto) n. l. R.C. Church, the beads at the ends of each decade of the rosary marking the points at which the Paternoster is recited. 2. any fixed form of words used as a prayer or charm. I Also called paterupster lige, a type of fishing tackle in which short lines and hooks are attached at intervals to the main line. 4 a type of lift in which platforms are attached to continuous chains. The lift does not stop at each floor but passengers emer while it is moving. (Latin, Merally: our father (from the opening of the Lord's Prayer)]

Paternoster (perto unsto) a. (sometimes not cap.) R.C. Church. L. the Lord's Prayer, esp. in Latin. 2. the recital of this as an act of devotion. [see PATERMOSTER]

Paterson' ('pazies'n) n. a city in NE New Jersey: settled by the Dutch in the late 17th century. Pop.: 139 160 (1986 est.).

Paterson' ('patos'n) n. 1. Andrew Barton, known as Banjo Paterson, 1884-1941, Australian poet. His works include "Waltzing Marida" and "The Man from Snowy River". 2 William. 1658-1719. Scottish merchant and banker: founded the Bank of England (1694). Paterson's curse in an Australian name for viper's bugies.

path (pa:8) n., pl. paths (pa:0z). L a road or way, esp. a narrow trodden track. 2 a surfaced walk, as through a garden. & the course or direction in which something moves: the path of a whiriwind 4. a course of conduct: the path of virtue. [Old English path; related to Old High German, German Pind] — pathless adj. path. (p.ef) abbrev. for: 1. pathological. I. pathology.

-path n. combining form. L. denoting a person suffering from a specified disease or disorder: neuropath. L. denoting a practitioner of a particular method of treatment orteopath. [back formation [YHTK4- MOO]

Pathen (policin) in a member of the Pashto-speaking people of Afghanistan, NW Pakistan, and elsewhere, most of whom are Muslim in religion. [C17: from Hindi]

pathetic (po'Getrk) add. 1. evoking or expressing pity, sympathy. etc. 2. distressingly inadequate; the old man sat huddled in front of a pathetic fire. 3. Brit informal, judicrously or contemptibly uninteresting or worthless: the standard of goalkeeping in amateur. football today is pathetic. 4. Obsolete, of or affecting the feelings! -pl. n. 5. pathetic sentiments. [C16: from French pathetique, via Late Latin from Greek pathetikas sensitive, from pathas suffering see PATROS] -pa'thetically adv.

pathetic fallacy n. (in literature) the presentation of manimate objects in nature as possessing human feelings.

pathfinder ('pag,fainds) n. L. a person who makes or finds a way.

esp. through unexplored areas or fields of knowledge. 3. an aircraft or parachutist who indicates a target area by dropping flores, etc. 3. a radar device used for cavigation or homing onto a target! -'path, finding n.

pathic ('pask) n. 1, a catamite. 2, a person who suffers; victim ~adj. 3. of or relating to a catemite. 4 of or relating to suffering. [C17: via Latin from Greek pathikes passive; see PATHOS]

patho- or before a vowel Dath- combining form. disease: pathoty pathogen ('pæ0s,d3cn) or pathogene ('pæ0s,d3l:n) n. any agent that can cause disease.

pathogenesis (,pæ95'dgenmis) or pathogeny (p5'86dgial) ii. the releament, and resultant enects of a suscesse. genetic (pætoudgi netik) adi.

pathogenic (,pedo'dgenik) add able to cause or produce disease. pathogenic bacteria.

pathognomenic (pedogno'mpnik) adj. Pathol. characteristic of. indicative of a particular discuse. (C17: from Greak paths) gnomonikos expert in judging lilness, from PATRO- + gromos judges - pathogno menically odv.

pathognomy (poleognami) is study or knowledge of the pastions of emotions or their manifestations. [C18: from PATHO- + -gnomy, to it. PHYSIOGNOMY]

pathol. abbrev. for: 1. pathological, 2. pathology. pathological (persolodatk') or (less commonly) pathologic I. of or relating to pathology. E relating to, involving, or caused disease. 3. Informat computatively motivated: a pathological factor pathological factor. -, patho'logically adv. pathology (paibplod31) A., pl. -gies. 1. the branch of medicinity

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ANNEXIB

SHORT REPORT

Strain- and Genotype-Specific Differences in Virulence of Paenibacillus larvae subsp. larvae, a Bacterial Pathogen Causing American Foulbrood Disease in Honeybees

Elke Genersch, 1* Ainura Ashiralieva, 1 and Ingemar Fries2

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Received 4 May 2005/ Accepted 23 June 2005

Virulence variations of Paenibacillus larvae subsp. larvae, the causative agent of American foulbrood disease of honeybees, were investigated by analysis of 16 field isolates of this pathogen, belonging to three previously characterized genotypes, as well as the type strain (ATCC 9545) of P. larvae subsp. larvae, with exposure bioassays. We demonstrated that the strain-specific 50% lethal concentrations varied within an order of magnitude and that differences in amount of time for the pathogen to kill 100% of the infected hosts (LT₁₀₀) correlated with genotype. One genotype killed rather quickly, with a mean LT₁₀₀ of 7.8 ± 1.7 days postinfection, while the other genotypes acted more slowly, with mean LT₁₀₀s of 11.2 ± 0.8 and 11.6 ± 0.6 days postinfection.

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Summary of full report

Oxytetracycline sensitivity of Paenibacillus larvae. subsp. larvae isolates

by Michael Hornitzky

January 2005

RIRDC Publication No 05/021 RIRDC Project No DAN-219A

Executive summary

American foulbrood (AFB), caused by Paenibacillus larvae subsp. larvae, is considered to be the most important bacterial disease of honey bees in Australia. In many countries oxytetracycline hydrochloride (OTC) is used to treat the disease. On mainland Australia AFB is controlled by the incineration of infected hives or the irradiation of hive material from diseased hives. Tasmania is the only state which permits treatment with OTC.

In recent years OTC-resistant P. I. larvae have emerged in the United States of America, Canada and Argentina. There is no information on the OTC sensitivity of P. I. larvae in Australian bees and whether honey imported from overseas (Argentina) contains OTC-resistant P. I. larvae. This information is important as it has a bearing on future control options for bacterial honey bee diseases in Australia.

This study has demonstrated that P. I. larvae isolated from Australian sources are very sensitive to OTC and that no resistance to OTC appears to have developed over the past 15/16 years. Most isolates from imported honey had higher minimum inhibitory concentrations for OTC than Australian isolates but the difference was so minor that they would all still be considered to be very sensitive to OTC.

This indicates that honey imported from Argentina has not been a significant source of OTC-resistant P. I. larvae.

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DSMZ - List of Microbial Species: Paenibacillus larvae subsp. larvae (Bacteria)

DSMZ

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Name	Paenibacillus larvae subsp. larvae (White 1906) Ash et al. 1994 emend. Heyndrickx et al. 1996 ^{VP} - see also <u>Bacterial Nomenclature Up-to-Date</u>
Synonym	Bacillus larvae
Restrictions	Animal pathogen, restricted distribution (F)
Strains	7030

DSMZ Microorganisms